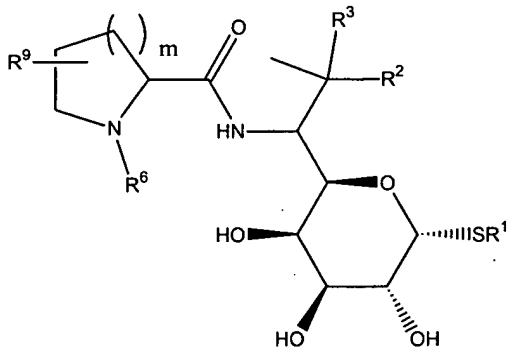
AMENDMENTS TO THE SPECIFICATION

Please replace paragraph **[0006]** with the following amended paragraph:

[0006] In one of its composition aspects, this invention is directed to a compound of formula (I):



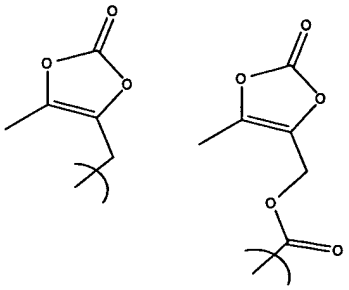
(I)

wherein:

R^1 is alkyl;

R^2 and R^3 are independently H, alkyl, hydroxy, fluoro, or cyanoalkyl or one of R^2 and R^3 is $=NOR^7$ and the other is absent, or one of R^2 and R^3 is $=CH_2$ and the other is absent, with the provisos that both R^2 and R^3 are not H; when one of R^2 and R^3 is fluoro, the other is not hydrogen or hydroxy; and when one of R^2 and R^3 is hydroxy, the other is not fluoro, hydrogen, or hydroxy;

R^6 is selected from the group consisting of H, alkyl, hydroxyalkyl, -C(O)O-alkylene-cycloalkyl, -C(O)O-alkylene-substituted cycloalkyl, -C(O)O-alkyl, -C(O)O-substituted alkyl, -C(O)O-aryl, -C(O)O-substituted aryl, -C(O)O-heteroaryl, -C(O)O-substituted heteroaryl, $-[C(O)O]_p$-alkylene-heterocycle, $-[C(O)O]_p$-alkylene-substituted heterocycle, wherein p is 0 or 1 with the proviso that -C(O)O-substituted alkyl does not include the following:



R^7 is H or alkyl;

R^9, which can be singly or multiply substituted in the ring on the same or different carbons, is independently selected from the group consisting of ~~hydrogen,~~ alkyl, substituted alkyl, alkoxyalkoxy, cycloalkyl, substituted cycloalkyl, alkoxyalkoxy, substituted oxygen, substituted nitrogen, halogen, phenyl, substituted phenyl, $-(CH_2)_n$-OH, $-(CH_2)_n$-NR^4R^5, -alkylene-R^a where R^a is selected from monofluorophenyl and monochlorophenyl, and branched chain isomers thereof wherein n is an integer of from 1 to 8 inclusive and R^4 and R^5 are H or alkyl; and

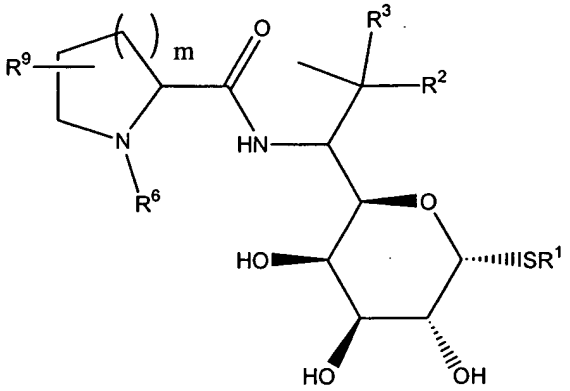
m is 1 or 2; and

prodrugs, tautomers or pharmaceutically acceptable salts thereof;

with the proviso that the compound of formula I has a minimum inhibition concentration of 32 μg/mL or less against at least one of the organisms selected from the group consisting of *Streptococcus pneumoniae, Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus faecalis, Enterococcus faecium, Haemophilus influenzae, Moraxella catarrhalis, Escherichia coli, Bacteroides fragilis, Bacteroides thetaiotaomicron, and Clostridium difficile.*

Please replace paragraph **[0007]** with the following amended paragraph:

[0007] In a preferred embodiment, this invention provides compounds of formula (II)



(II)

wherein:

R^1 is alkyl;

R^2 and R^3 are independently H, alkyl, or cyanoalkyl, with the proviso that both R^2 and R^3 are not H;

R^6 is H, alkyl, or hydroxyalkyl;

R^9, which can be singly or multiply substituted in the ring on the same or different carbons, is independently selected from the group consisting of ~~hydrogen~~, alkyl, substituted alkyl, alkoxyalkoxy, cycloalkyl, substituted cycloalkyl, alkoxyalkoxy, substituted oxygen, substituted nitrogen, halogen, phenyl, substituted phenyl, $-(CH_2)_n-OH$, $-(CH_2)_n-NR^4R^5$, -alkylene-R^a where R^a is selected from monofluorophenyl and monochlorophenyl, and branched chain isomers thereof wherein n is an integer of from 1 to 8 inclusive and R^4 and R^5 are H or alkyl; and

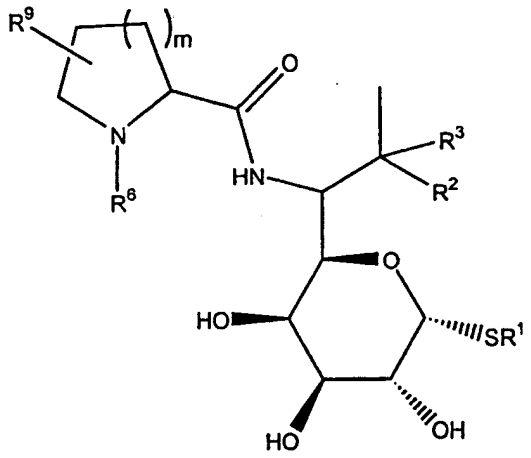
m is 1 or 2; and

prodrugs and pharmaceutically acceptable salts thereof;

with the proviso that the compound of formula II has a minimum inhibition concentration of 32 μg/mL or less against at least one of the organisms selected from the group consisting of *Streptococcus pneumoniae, Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus faecalis, Enterococcus faecium, Haemophilus influenzae, Moraxella catarrhalis, Escherichia coli, Bacteroides fragilis, Bacteroides thetaiotaomicron, and Clostridium difficile.*

Please replace paragraph **[0008]** with the following amended paragraph:

[0008] In a particularly preferred embodiment, this invention provides compounds of formula (III):



(III)

wherein:

R^1 is alkyl;

R^2 and R^3 are fluoro;

R^6 is H, alkyl, or hydroxyalkyl;

R^9, which can be singly or multiply substituted in the ring on the same or different carbons, is independently selected from the group consisting of ~~hydrogen,~~ alkyl, substituted alkyl, alkoxyalkoxy, cycloalkyl, substituted cycloalkyl, alkoxyalkoxy, substituted oxygen, substituted nitrogen, halogen, phenyl, substituted phenyl, $-(CH_2)_n$-OH, $-(CH_2)_n$-NR^4R^5, -alkylene-R^a where R^a is selected from monofluorophenyl and monochlorophenyl, and branched chain isomers thereof wherein n is an integer of from 1 to 8 inclusive and R^4 and R^5 are H or alkyl; and

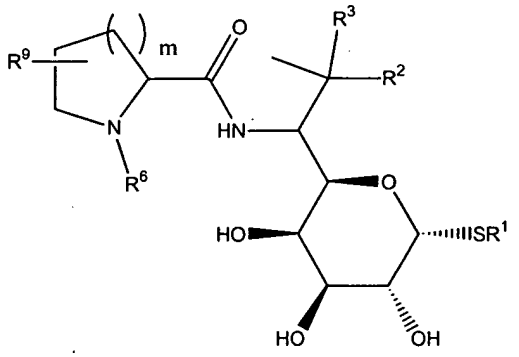
m is 1 or 2; and

prodrugs and pharmaceutically acceptable salts thereof,

with the proviso that the compound of formula III has a minimum inhibition concentration of 32 μg/mL or less against at least one of the organisms selected from the group consisting of

Streptococcus pneumoniae, Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus faecalis, Enterococcus faecium, Haemophilus influenzae, Moraxella catarrhalis, Escherichia coli, Bacteroides fragilis, Bacteroides thetaiotaomicron, and Clostridium difficile.

In another preferred embodiment, this invention is directed to a compound of formula (IV):



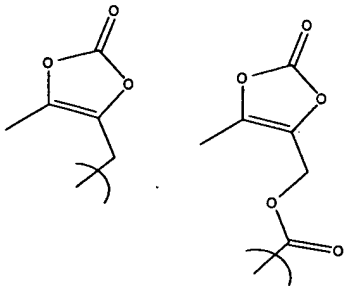
(IV)

wherein:

R^1 is alkyl;

R^2 and R^3 are independently H, or alkyl, hydroxy, fluoro, or cyanoalkyl or one of R^2 and R^3 is $=NOR^7$ and the other is absent, or one of R^2 and R^3 is $=CH_2$ and the other is absent, with the provisos that both R^2 and R^3 are not H; when one of R^2 and R^3 is fluoro, the other is not hydrogen or hydroxy; and when one of R^2 and R^3 is hydroxy, the other is not fluoro, hydrogen, or hydroxy;

R^6 is selected from the group consisting of -C(O)O-alkylene-cycloalkyl, -C(O)O-alkylene-substituted cycloalkyl, -C(O)O-alkyl, -C(O)O-substituted alkyl, -C(O)O-aryl, -C(O)O-substituted aryl, -C(O)O-heteroaryl, -C(O)O-substituted heteroaryl, $-[C(O)O]_p$-alkylene-heterocycle, $-[C(O)O]_p$-alkylene-substituted heterocycle, wherein p is 0 or 1 with the proviso that -C(O)O-substituted alkyl does not include the following:



R^7 is H or alkyl;

R^9, which can be singly or multiply substituted in the ring on the same or different carbons, is independently selected from the group consisting of ~~hydrogen,~~ alkyl, substituted alkyl, alkoxyalkoxy, cycloalkyl, substituted cycloalkyl, alkoxyalkoxy, substituted oxygen, substituted nitrogen, halogen, phenyl, substituted phenyl, $-(CH_2)_n$-OH, $-(CH_2)_n$-NR^4R^5, -alkylene-R^a where R^a is selected from monofluorophenyl and monochlorophenyl, and branched chain isomers thereof wherein n is an integer of from 1 to 8 inclusive and R^4 and R^5 are H or alkyl; and

m is 1 or 2; and

prodrugs, tautomers or pharmaceutically acceptable salts thereof;

with the proviso that the compound of formula I has a minimum inhibition concentration of 32 μg/mL or less against at least one of the organisms selected from the group consisting of *Streptococcus pneumoniae, Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus faecalis, Enterococcus faecium, Haemophilus influenzae, Moraxella catarrhalis, Escherichia coli, Bacteroides fragilis, Bacteroides thetaiotaomicron, and Clostridium difficile.*

Please replace paragraph **[0010]** with the following amended paragraph:

[0010] ~~As used below, these compounds are named based on acetamide or amide derivatives but, alternatively, these compounds could have been named based on 1-thio-L-threo-β-D-galacto-octopyranoside derivatives.~~ Specific compounds within the scope of this invention include the following compounds:

~~1-(4-ethylpiperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-ethyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(-4-n-propyl-N-methylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 1-methyl-4-propyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide ;

~~1-(-4-n-propyl-N-methylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methyl-3-cyanoprop-1-yl}acetamide~~ 1-methyl-4-propyl-pyrrolidine-2-carboxylic acid [3-cyano-2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(-4-ethylpiperidyl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-hydroxy-2-methylprop-1-yl}acetamide~~ 4-ethyl-piperidine-2-carboxylic acid [2-hydroxy-2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(-4-n-propyl-N-methylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-hydroxyiminoprop-1-yl}acetamide~~ 1-methyl-4-propyl-pyrrolidine-2-carboxylic acid [2-hydroxyimino-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(-4-n-propyl-N-methylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methoxyiminoprop-1-yl}acetamide~~ 1-methyl-4-propyl-pyrrolidine-2-carboxylic acid [2-methoxyimino-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(-3-n-butylpiperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 5-butyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-n-pentylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-pentyl-pyrrolidine-2-

carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-(3-methylbut-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3-methyl-butyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-n-pentylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-n-propyl-N-methylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2,2-difluoroprop-1-yl}acetamide~~ 1-methyl-4-propyl-pyrrolidine-2-carboxylic acid [2,2-difluoro-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-n-pentylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2,2-difluoroprop-1-yl}acetamide~~ 4-pentyl-pyrrolidine-2-carboxylic acid [2,2-difluoro-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-(3-p-fluorophenyl)prop-1-ylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-[3-(4-fluoro-phenyl)-propyl]-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-(3,3-difluoroprop-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3,3-difluoro-propyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-(3-p-chlorophenyl)prop-1-ylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-[3-(4-chloro-phenyl)-

propyl]-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-(2,2-difluoropent-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(2,2-difluoro-pentyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-n-propylpiperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-propyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-n-pentyl-N-(2-hydroxyeth-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 1-(2-hydroxy-ethyl)-4-pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-n-pentyl-N-(2-(R)-methyl-2-hydroxyeth-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 1-(2-hydroxy-propyl)-4-pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-n-pentyl-N-(2-(S)-methyl-2-hydroxyeth-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 1-(2-hydroxy-propyl)-4-pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-n-pentyl-N-(3-hydroxyprop-1-yl)pyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 1-(3-hydroxy-propyl)-4-pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-(3-methylbut-1-yl)-N-(2-hydroxyeth-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 1-(2-

hydroxy-ethyl)-4-(3-methyl-butyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-(3,3-difluoroprop-1-yl)-N-(2-hydroxyeth-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3,3-difluoro-propyl)-1-(2-hydroxy-ethyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-n-pentyl-N-(2-hydroxyeth-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2,2-difluoroprop-1-yl}acetamide~~ 1-(2-hydroxy-ethyl)-4-pentyl-pyrrolidine-2-carboxylic acid [2,2-difluoro-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-n-pentylpiperid-6-yl)-N-{[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-pentyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-(1-ethylprop-1-yl)piperid-6-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(1-ethyl-propyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-iso-propylpiperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-isopropyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-n-butylpiperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-butyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-cyclohexylpiperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-cyclohexyl-piperidine-

2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-ethyl-N-hydroxyethyl-piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-ethyl-1-(2-hydroxy-ethyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-n-pentyl-N-hydroxyethyl-piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 1-(2-hydroxy-ethyl)-4-pentyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-n-propyl-N-hydroxyethyl-piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 1-(2-hydroxy-ethyl)-4-propyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-n-propyl-N-(F-moc)-piperid-6-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 2-[2-Methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propylcarbamoyl]-4-propyl-piperidine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester;

~~1-[4-n-propyl-N-(carboxylic acid ethyl ester)-piperid-6-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 2-[2-Methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propylcarbamoyl]-4-propyl-piperidine-1-carboxylic acid ethyl ester;

~~1-[4-n-propyl-N-(carboxylic acid phenyl ester)-piperid-6-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 2-[2-Methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propylcarbamoyl]-4-propyl-piperidine-1-carboxylic acid phenyl ester;

~~1-[4-(4,4-difluoropent-1-yl)-pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(4,4-difluoro-pentyl)-

pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-(3,3-difluorobut-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3,3-difluoro-butyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-(3,3-difluoropent-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3,3-difluoro-pentyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-(3,3-difluoropent-1-yl)-N-(2-hydroxyeth-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3,3-difluoro-pentyl)-1-(2-hydroxy-ethyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-(2,2-difluoroeth-1-yl)piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3,3-difluoro-propyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-(3,3-difluoroprop-1-yl)piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(4,4-difluoro-butyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-(5,5-difluoropent-1-yl)piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(5,5-difluoro-pentyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-(5-fluoropent-1-yl)piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(5-fluoro-pentyl)-

piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-(4-fluorobut-1-yl)piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(4-fluoro-butyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-(3-ethyl-3-hydroxypent-1-yl)piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3-ethyl-3-hydroxy-pentyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-butoxypiperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-butoxy-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-pentoxypiperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-pentyloxy-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-(4-fluorobutoxy)piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(4-fluoro-butoxy)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-n-butylprop-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methyl-allyl}acetamide~~ 4-butyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-allyl]-amide;

~~1-(4-ethyl-N-ethyl-piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 1,4-diethyl-piperidine-2-

carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-(3-fluoropropoxy)piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3-fluoro-propoxy)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-(3,3,3-trifluoropropoxy)piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3,3,3-trifluoro-propoxy)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-iso-butylpiperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-isobutyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-(4-n-propylpiperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2,2-difluoro-prop-1-yl}acetamide~~ 4-propyl-piperidine-2-carboxylic acid [2,2-difluoro-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-n-propyl-4-fluoro-pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-fluoro-4-propyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~1-[4-n-butyl-4-fluoro-pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-butyl-4-fluoro-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

4-Fluoro-4-propyl-pyrrolidine-2-carboxylic acid [2-hydroxy-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

~~4-Fluoro-4-propyl-pyrrolidine-2-carboxylic acid [2-hydroxy-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amid; and~~ 4-(2-methoxyethoxy)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide;

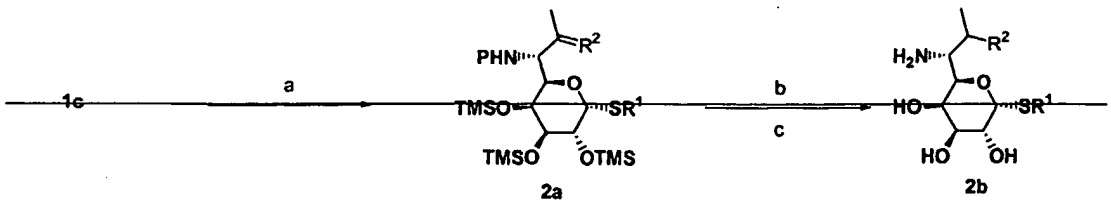
and prodrugs, tautomers and pharmaceutically acceptable salts thereof.

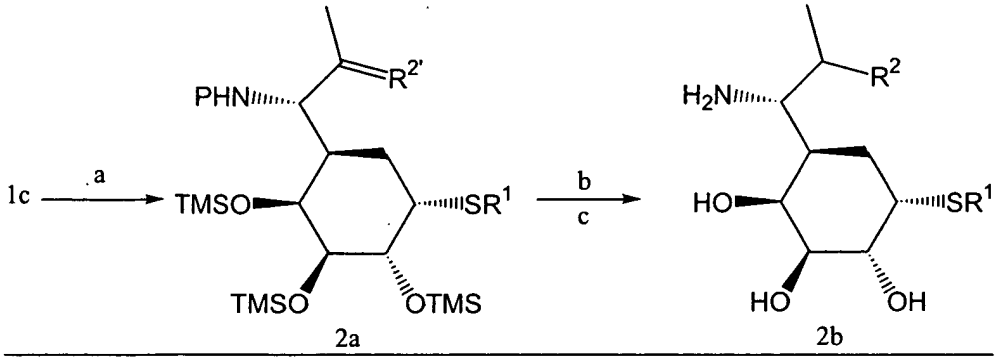
Please replace paragraph **[0068]** with the following amended paragraph:

[0068] The 7-O-trimethylsilyl group of **1b** is chemoselectively deprotected and oxidized to provide the 7-keto-lincosamine derivative **1c**. This selective transformation is performed by addition of the protected product **1b** to dimethylsulfoxide and oxalyl chloride in an inert organic solvent such as dichloromethane followed by an appropriate organic base such as triethylamine. Alternatively, the transformation may be performed by addition of **1b** to dimethyl sulfoxide and an appropriate activating agent such as trifluoroacetic anhydride in an inert organic solvent. The reaction is typically conducted at temperatures in the range of approximately [[-70°C to 80°C]] <u>-70 °C to -80 °C</u>. The resulting reaction mixture is stirred at the low temperature and is then allowed to warm to approximately -50°C. The reaction is maintained at this second temperature for approximately 1 h to 3 h. To the reaction mixture is added a suitable organic base, such as TEA, pyridine, and the like. The reaction mixture is appropriately worked up to provide the product **1c**. The general class of conditions used in the transformation of **1b** to **1c** is known in the art as Swern oxidation conditions

Please replace paragraph **[0069]** with the following amended paragraph:

[0069] Scheme 2 below illustrates a general synthesis of a lincosamine intermediate **2b** wherein P is an N-protecting group, preferably either Cbz or Boc, R^1 is as defined for formula (I), and one of R^2 and R^3 is hydrogen and the other is as defined for formula (I).





Scheme 2. General synthesis of lincosamine intermediate **2b**.

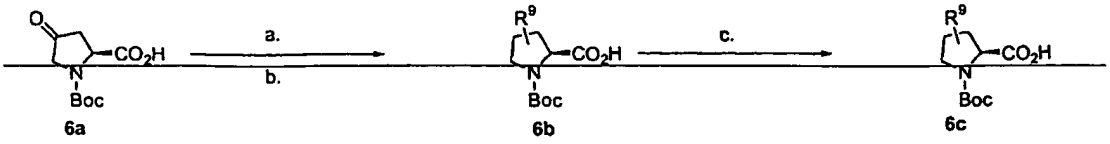
(a) Wittig olefination ($R^2PPh_3^+X^-$, $R^2PO(OEt)_2$, base, solvent); (b) and (c) H_2/Pd, Global de-protection

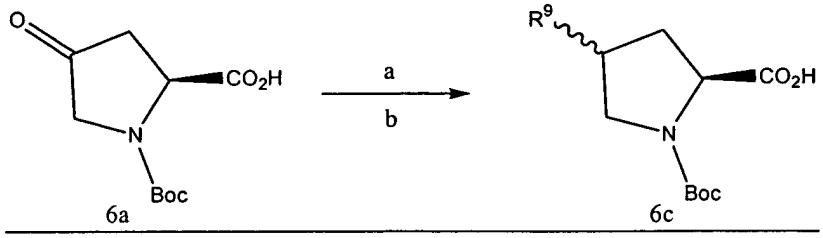
Please replace paragraph **[0073]** with the following amended paragraph:

[0073] The product **2a** is then hydrogenated to provide the saturated product **2b**. The hydrogenation is typically performed in a polar organic solvent such as methanol, ethanol, and the like, using 10% palladium on carbon in a Parr bottle. The bottle is purged, and charged with H_2 to approximately 50 to 70 psi and shaken until completion, typically approximately 12 to 24 h. The resulting reaction mixture is filtered, *e.g.*, through celite, and rinsed with a polar organic solvent such as methanol. The organic solution is worked up by transferring to a resin funnel containing dry, washed ~~Dowex~~ Dowex™ 50w-400x H^+ form and shaken. After washing the resin with methanol and water, the product **2b** is eluted from the resin by washing with 5% TEA in MeOH. The product can also be purified by silica gel column chromatography.

Please replace paragraph **[0084]** with the following amended paragraph:

[0084] Scheme 6 below illustrates a general synthesis of a proline intermediate **6c** wherein R^9 is as defined for formula (I).





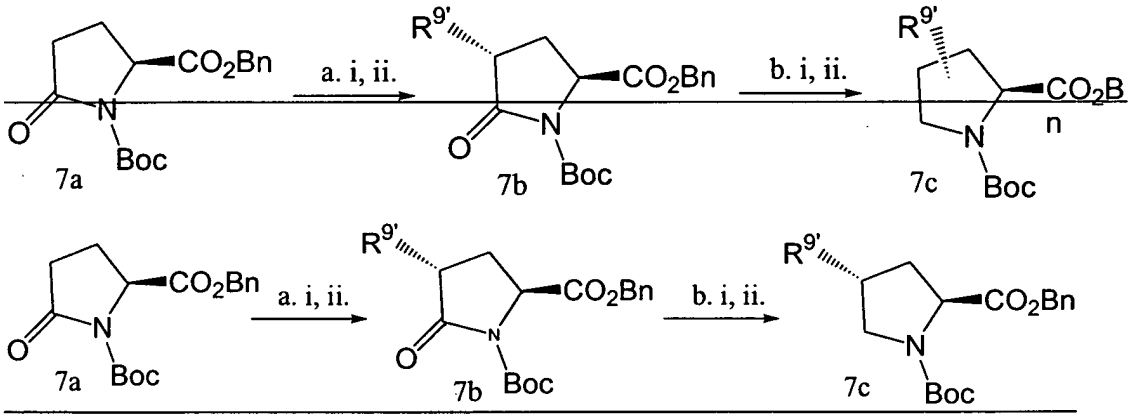
Scheme 6. General synthesis of *cis/trans* R^9-proline intermediate mixtures **6c**.
(a) ~~$R^9CH_2Br+Ph_3P$~~ $R^9P^+PH_3Br^-$, NaH, DMSO; (b) H_2/Pt

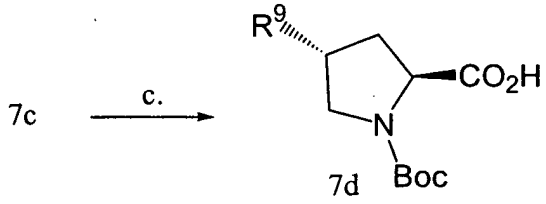
Please replace paragraph **[0085]** with the following amended paragraph:

[0085] As shown in Scheme 6, the product **6c** is prepared as described in Magerlein ~~Birkenmeyer, *et al.*~~, *Journal of Medicinal Chemistry* **1972**, *15*, 1255-1259. Compound **6a** is commercially available from vendors such as RSP (Scientific Research Consortium, Inc.). Alternatively, **6a** can be prepared from commercially available protected hydroxy prolines by methods well known in the art. See, *e.g.*, Demange, *et al.*, *Tetrahedron Letters* **1998**, *39*,1169-1172.

Please replace paragraph **[0086]** with the following amended paragraph:

[0086] Scheme 7 below illustrates a general synthesis of trans-R^9-proline intermediates **7d**, wherein R^9 is alkyl or substituted alkyl.





Scheme 7. General synthesis of *trans*-alkylprolines **7d**.

(a) (i) LiHMDS, THF -78°C, (ii) bromoalkene; (b) (i) $LiBHEt_3$, THF -78°C, (ii) BF_3OEt_2, Et_3SiH; (c) [[H2]] $\underline{H_2}$ Pd/C.

Please replace paragraph **[0169]** with the following amended paragraph:

[0169] Triphenylphosphonium bromide (3.29 g, 9.2 mmol) and potassium *tert*-butoxide (715 mg, 6.4 mmol) under N_2 atmosphere were suspended in toluene (31 mL) with vigorous stirring. After 4 h protected product **1c** (P=Cbz, R^1=Me) (1.4 g, 2.36 mmol) in toluene (20 mL) was added by cannula. The resulting reaction mixture was stirred 2 h and then diluted with EtOAc (250 mL). The resulting organic solution was washed quickly with H_2O (2 x 100 mL), brine (1 x 100 mL) dried over Na_2SO_4 and evaporated to dryness. Chromatography of the crude product on silica 6% EtOAc/Hexanes containing 0.2% TEA gave the alkene product **2a** (P=Cbz, R^1=Me, [[R^2]]$\underline{R^{2'}}$ =CH_2) as a colorless oil that crystallized after co-evaporation from toluene and cyclohexane (0.65 g, 46%).

Please replace paragraph **[0171]** with the following amended paragraph:

[0171] The product **2a** (P=Cbz, R^1=Me, [[R^2]]$\underline{R^{2'}}$=CH2) (490 mg, 0.82 mmol) in ethanol (50 mL) was added to 10% palladium on carbon (Degussa wet form 50% w/w water) (700 mg) in a par bottle. The bottle was purged, and charged with H_2 to 65 psi and shaken 24 h. The reaction mixture was filtered through celite, rinsed with methanol. The organic solution was transferred to a resin funnel containing dry, washed ~~Dowex~~ Dowex™ 50w-400x H^+ form (0.8 g) and shaken for 10 min. After washing the resin with methanol three times and water two times, the saturated product **2b** (R^1 =Me, R^2=Me) was eluted from the resin by washing with 5% TEA in MeOH (35 mL, x 10 min x 5). The combined filtrate was evaporated to dryness, co-evaporated from EtOH twice and lyophilized from 1:1 MeCN/H_2O to give the product as a colorless powder (198.4 mg 96%).

Please replace paragraph **[0173]** with the following amended paragraph:

[0173] In the alternative when a Boc-protecting group is used, methyltriphenylphosphonium bromide (12 g, 33.6 mmol) and potassium *t*-butoxide (3g, 26.7 mmol) were taken in THF (70 mL) at 0°C, and stirred at rt for 4 h. Then Boc-protected product **1c** (P=Boc, R^1=Me) (4.7 g, 8.2 mmol) in THF (30 mL) was added and stirred at rt for 2 h. After which it was extracted with EtOAc (300 mL), washed with brine (100 mL) and dried over sodium sulfate. The crude alkene product **2a** (P=Boc, R^1=Me, $[[R^2]]\underline{R^{2'}}$=$CH_2$) was purified on silica gel column chromatography using 10% EtOAc in Hexane as eluent (4.1 g, 87.6%).

Please replace paragraph **[0175]** with the following amended paragraph:

[0175] To the product **2a** (P=Boc, R^1=Me, $[[R^2]]\underline{R^{2'}}$=$CH_2$) in methanol (30 mL), ~~Dowex~~ Dowex™ H^+ resin (1 g) was added and stirred at rt for 1 h. The resin was filtered and the product obtained on removal of solvent (2.4 g, 6.8 mmol,) was taken in MeOH (30 mL). Pd/C (2.5 g) was added and hydrogenated at 55 psi overnight. The crude product obtained on filtering and removal of solvent was purified on silica gel column chromatography using 10% MeOH in DCM to provide Boc-protected 7-Methyl MTL as a white solid (2.06 g, 86%). TLC R_f= 0.5 (10% of MeOH in DCM).

Please replace paragraph **[0178]** with the following amended paragraph:

[0178] Sodium hydride (80 mg, 3.3 mmol) under N_2 atmosphere was suspended in THF (4 mL) with vigorous stirring. The suspension was cooled to -30°C and diethyl(cyanomethyl)phosphonate (805 μL, 5.0 mmol) was added. After 30 min protected product **1c** (P=Cbz, R^1=Me) (1.0 g, 1.7 mmol) in THF (3 mL) was added by cannula. The resulting reaction mixture was stirred 4 h and then diluted with EtOAc (250 mL). The resulting organic solution was washed quickly saturated aqueous $NaHCO_3$ (1 x 100 mL), brine (1 x 50 mL) dried over Na_2SO_4 and evaporated to dryness. Chromatography of the crude product on silica 6% EtOAc/Hexanes to 10% EtOAc/Hexanes containing 0.2% TEA gave the protected alkene product **2a** (P=Cbz, R^1=Me, $[[R^2]]\underline{R^{2'}}$=CHCN) as a colorless oil (0.38 g, 37%). MS(ESPOS): 625.5.2 [M+H], ES(NEG): 659.5 [M+Cl].

Please replace paragraph **[0179]** with the following amended paragraph:

[0179] The product **2a** (P=Cbz, R^1=Me, [[R^2]]$\underline{R^{2'}}$=CHCN) (180 mg, 0.29 mmol) in ethanol (15 mL) was added to 10% palladium on carbon (Degussa wet form 50% w/w water) (300 mg) in a Parr bottle and concentrated HCl (29 μL) was added. The bottle was purged, and charged with H_2 to 65 psi and shaken for 24 h. The reaction mixture was filtered through celite, rinsed with methanol. The organic solution was transferred to a resin funnel containing dry, washed ~~Dowex~~ Dowex™ 50w-400x H^+ form (1 g) and shaken 10 min. After washing the resin with methanol twice and water, the saturated product **2b** (R^1=Me, R^2=CH_2CN) was eluted from the resin by washing with 5% TEA in MeOH (20 mL x 20 min x 3) and MeCN (20 mL x 20 min). The combined organic filtrate was evaporated to dryness lyophilized from 1:1 MeCN/H_2O to give the product **2b** (R^1=Me, R^2=CH_2CN) as a colorless solid (70 mg, 91%). ES(NEG): 275.3 [M-H].

Please replace paragraph **[0194]** with the following amended paragraph:

[0194] TLC: R_f= 0.3 [Solvent system: DCM:hexanes:MeOH(6:5:1)]. MS(ESNEG ~~NEGATIVE~~): 284.5 $[M-H]^-$.

Please replace paragraph **[0206]** with the following amended paragraph:

[0206] To a solution of [[**8a**]] **8b** ($R^{9'}$=3,3-difluoroprop-2-enyl) (126 mg, 0.33 mmol) in MeOH (35 mL) was added 10% palladium on carbon (Degussa wet form 50% w/w water) (120 mg). The reaction mixture was stirred at rt under hydrogen (1 atm) overnight and was filtered through celite with the aid of MeOH. The filtrate was concentrated to give a clear syrup **8c** (R^9=3,3-difluoropropyl) (97 mg, 100%).

Please replace paragraph **[0208]** with the following amended paragraph:

[0208] [[**[0202]**]]To a solution of aldehyde [[**8b**]] **8a** (258 mg, 0.74 mmol, 1 equiv) in THF (3 mL) at 0°C was added tetraallyltin (178 μL, 0.74 mmol, 1 equiv), followed by the drop-wise addition of boron trifluoride etherate (94.3 μL, 0.74 mmol, 1 equiv) over a period of 15 min. The reaction mixture was stirred at 0°C for 1.5 h. Then a solution of potassium fluoride (125 mg) in water (1.25 mL) was added. The resulting mixture was warmed to rt and stirred at rt for 20 min.

This was followed by the addition of methanol (10 mL) and the resulting mixture was stirred at rt for another 20 min. The reaction mixture was filtered over celite. The filtrate was evaporated to dryness. The residue was diluted with dichloromethane (100 mL), washed with water (50 mL), dried, concentrated and purified by chromatography to give a clear oil **9a** (R^9=2-hydroxypent-4-enyl) (261 mg, 90%): MS(ESPOS): 412.5 $[M + NA]^+$, 290.4 $[M - Boc + H]^+$.

Please replace paragraph **[0214]** with the following amended paragraph:

[0214] To 4-propylpyridine (2.5 g, 20 mmol), 30% hydrogen peroxide (2.4 g) was added and refluxed overnight. The solvent was removed and the resulting residue was taken in DCM (30 mL). Trimethylsilyl cyanide (2.6 g, 26 mmol) was added to the above solution followed by dimethylcarbamyl chloride (2.8 g, 26 mmol), and the reaction mixture was stirred at rt overnight. Potassium carbonate (10%, 100 mL) was added. The organic layer was separated, dried over sodium sulfate and then concentrated to obtain 4-propyl-2-cyanopyridine (2.5 g, 93%). ~~It was then refluxed in~~ The crude nitrile was dissolved in aqueous hydrochloric acid (6N, 60 mL) ~~for~~ and refluxed overnight. The 4-propyl-2-carboxylic acid pyridine **10b** (R^9=propyl) was obtained after crystallization from acetonitrile (2g, 71%)

Please replace paragraph **[0218]** with the following amended paragraph:

[0218] To a mixture of 7-Me MTL HCl salt **2b** (R^1=Me, R^2=Me) (200 mg, 0.69 mmol, 1 equiv) in dry DMF (1.8 mL) at 0 °C was added triethylamine (0.50 mL, 3.61 mmol, 5.2 equiv), followed by the addition of BSTFA (0.28 mL, 1.04 mmol, 1.5 equiv). The reaction mixture was stirred at 0 °C for 10 minutes, and then was stirred at rt for 50 minutes. To the reaction mixture was added the acid **13a** (341 mg, 0.90 mmol, 1.3 equiv) and HATU (423 mg, 1.11 mmol, 1.6 equiv). The reaction mixture was stirred at rt for 3 h. The reaction mixture was evaporated to dryness, taken up in ethyl acetate, washed with water (1 x), sat. $NaHCO_3$ (1 x) and brine. The organic layer was dried over Na_2SO_4 and evaporated to give a yellow residue which was dissolved in methanol (20 mL) to which was added dry ~~Dowex~~ Dowex™ resin (250 mg). The reaction mixture was stirred at rt for 1 h. The resin was removed by filtration and the crude product eluted with 2M ammonia in methanol. The methanolic eluent was evaporated, and the resulting residue was purified by chromatography to

provide a white solid **13b** (R^1=Me, R^2= Me, R^3=H) (250 mg, 75%): ^{1}H NMR (300 MHz, CD_3OD) δ 8.46 (d, *J* = 1.8, 1), 8.30 (d, *J* = 5.4, 1), 7.98 (dd, *J* = 1.8, 5.1, 1), 5.25 (d, *J* = 6.0, 1), 4.32-4.23(m, 2), 4.09 (dd, *J* = 5.7, 10.2, 1), 3.87 (d, *J* = 3.0, 1), 3.54 (dd, *J* = 3.3, 10.2, 1), 2.24-2.15 (m, 1), 2.11 (s, 3), 0.99-0.96 (m, 6); MS (ESPOS): 483.5 $[M + H]^+$; MS (ESNEG): 481.4 $[M - H]^-$.

Please replace paragraph **[0228]** with the following amended paragraph:

[0228] A solution of pyridine **11b** (m=2, R^1=Me, R^2=Me R^3=H, R^9=ethyl) (167 mg, 0.435 mmol) in 3:2 methanol/water (20 mL) was added to platinum(IV)oxide (339 mg, 0.521 mmol) in a Parr bottle. Concentrated HCl (52 μL, 0.52 mmol) was then added. The bottle was purged, and charged with H_2 to 65 psi and shaken for 24 h. The reaction mixture was filtered through celite and rinsed with methanol. The combined filtrate was evaporated to dryness and chromatographed on silica 88:12 to 80:20 dichloromethane: 0.25% ammonia in methanol to give 43 mg of a high R_f product and 49 mg of a mixed fraction. Chromatography of the low R_f fraction on fluorosil 84:16 to 80:20 dichloromethane: 0.25% ammonia in methanol provided the title compound ~~1-(6-(S)-4-(R)-ethylpiperid-6-yl)-*N*-{1-(R)-[2-(S)-3-(S),4-(S),5-(R)-trihydroxy-6-(R)-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ (21.9 mg, 12.9%), which was taken up in 1:1 acetonitrile:water (50 mL), 0.2μ millipore filtered, and cooled to 0°C. 1N HCl (67 μL) in water (20 mL) was added and re-lyophilized to provide the title compound HCl salt (24.0 mg) as a colorless powder.

Please replace paragraph **[0232]** with the following amended paragraph:

[0232] Lincosamine **2b** (R^1=Me, R^2=CH_2CN) (54.2 mg, 0.20 mmol) prepared by Method E was dissolved in DMF (0.7 mL). The reaction mixture was cooled to 0°C and triethylamine (170 μL, 1.2 mmol) and BSTFA (96 μL, 0.36 mmol) was added. The reaction mixture was allowed to warm to rt, and stirred at rt for 1 h. 4-*n*-Propylhygric acid prepared by the method of Hoeksema, *et al.*, *J. Am. Chem. Soc.*, **1967**, *89* 2448-2452 (66.4 mg, 0.32 mmol) and HATU (149 mg, 0.39 mmol) were added, and the mixture was stirred at rt for 3 h. DMF was removed and the residue was dissolved in DCM (100 mL), washed with saturated $NaHCO_3$ (30 mL) and brine (30 mL), and dried over sodium sulfate. The residue obtained by removing the solvent was dissolved in methanol (20 mL) and

treated with ~~Dowex~~ Dowex™ resin H^+ (300 mg) for 15 min. The crude product was eluted from the resin by washing with 5% TEA in MeOH (25 mL x 15 min x 2) and 5% TEA in MeCN (25 mL x 15 min). The combined eluent was evaporated to dryness and purified by silica gel column chromatography using 7% 0.25M NH_3 in methanol in dichloromethane as the eluent to provide the title compound (24 mg, 28%).

Please replace paragraph **[0242]** with the following amended paragraph:

[0242] Lincosamine intermediate **2b** (R^1=Me, R^2=Me), prepared by Method C, was dissolved in DMF (2 mL). Triethylamine (80 mg, 1 mmol) and BSTFA (307 mg, 1.1 mmol) were added, and the mixture was stirred at rt for 1.5 h. Next, fusaric acid (143 mg, 0.7 mmol) and HATU (184 mg, 0.5 mmol) were added, and the mixture was stirred at rt for 3 h. DMF was removed and the residue was dissolved in EtOAc (50 mL), washed with sodium bicarbonate (10%, 30 mL) and brine (30 mL), and dried over sodium sulfate. The residue obtained by removing the solvent was dissolved in methanol and treated with ~~Dowex~~ Dowex™ resin H^+ for 1 h. The crude product obtained by filtering the resin and removing the solvent was purified on silica gel column chromatography using 10% methanol in dichloromethane as the eluent to give the title compound (100 mg, 61%).

Please replace paragraph **[0256]** with the following amended paragraph:

[0256] Boc 4-*trans*-Pentylproline **7d** (R^9=*n*-pentyl) (179 mg, 0.631 mmol), HATU (299 mg, 0.789 mmol), and diethylisopropylamine (182 mg, 1.2 mmol) were added to lincosamine intermediate **5b** (R^1=Me) prepared by ~~Method H~~ method I (210 mg, 0.526 mmol) in DMF (3 mL) at 0°C. The mixture was stirred at rt overnight. After removing DMF, the residue was taken in ethyl acetate and washed with saturated bicarbonate (30 mL). The organic portion was then dried over sodium sulfate and the solvent was removed to obtain the crude product. The crude product was purified by column chromatography using 30% ethyl acetate in hexanes as the eluent (200 mg, 57%). Potassium carbonate (450 mg, 3.0 mmol) was added to the product (200 mg, 0.30 mmol) of the above reaction in methanol (3 mL) and water (1 mL), and the mixture was stirred at rt for 2 h. The solvent was removed and the residue obtained was taken in 30% trifluoroacetic acid in dichloroethane (10 mL) and dimethyl sulfide (0.5 mL) and stirred for 1 h. After removing the

solvent, the crude product obtained was purified by column using 10% methanol in dichloromethane as the eluent (10 mg, 90%).

Please replace paragraph **[0259]** with the following amended paragraph:

[0259] Trifluoroacetic acid (5 mL) and water (0.33 mL) were added to a solution of the above syrup in dichloromethane (15 mL) with methyl sulfide (0.33 mL). The reaction mixture was stirred at rt for 1 h. The solvent was removed under vacuum and co-evaporated with toluene twice. The residue was purified by chromatography to provide the title compound ~~1-(2-(S)-4-(R)-(3-*p*-fluorophenyl)prop-1-ylpyrrolidin-2-yl)-*N*-{1-(S)-[2-(S)-3-(S),-4-(S),-5-(R)-trihydroxy-6-(R)-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ (90 mg, 62%) as a white solid.

Please replace paragraph **[0262]** with the following amended paragraph:

[0262] Trifluoroacetic acid (5 mL) and water (0.33 mL) were added to a solution of the above syrup in dichloromethane (15 mL) with methyl sulfide (0.33 mL). The reaction mixture was stirred at rt for 1 h. The solvent was removed under vacuum and co-evaporated with toluene twice. The residue was purified by chromatography to provide the title compound ~~1-[2-(S)-4-(R)-(3,3-difluoroprop-1-yl)pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ (81 mg, 64%) as a white solid.

Please replace paragraph **[0265]** with the following amended paragraph:

[0265] Trifluoroacetic acid (3 mL) and water (0.2 mL) were added to a solution of the above syrup in dichloromethane (9 mL) with methyl sulfide (0.2 mL). The reaction mixture was stirred at rt for 1 h. The solvent was removed under vacuum and co-evaporated with toluene twice. The residue was purified by chromatography to provide the title compound ~~1-(2-(S)-4-(R)-(3-*p*-chlorophenyl)prop-1-ylpyrrolidin-2-yl)-*N*-{1-(S)-[2-(S)-3-(S),-4-(S),-5-(R)-trihydroxy-6-(R)-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ (41.6 mg, 42%) as a white solid.

Please replace paragraph **[0268]** with the following amended paragraph:

[0268] Trifluoroacetic acid (3 mL) and water (0.20 mL) were added to a solution of the above syrup in dichloromethane (9 mL) with methyl sulfide (0.20 mL). The reaction mixture was stirred at rt for 1 h. The solvent was removed under vacuum and co-evaporated with toluene twice. The residue was purified by chromatography to provide the title compound ~~1-[2-(S)-4-(S)-(2,2-difluoropent-1-yl)pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ (56 mg, 62%) as a white solid.

Please replace paragraph **[0270]** with the following amended paragraph:

[0270] Triethylamine (0.18 mL, 1.26 mmol) and BSTFA (0.549 mL, 2.1 mmol) were added to the lincosamine intermediate **2b** (R^1=Me, R^2=Me) prepared by Method D (102 mg, 0.42 mmol) in DMF (5 mL) at 0°C, and the mixture was stirred at rt for 3 h. Acid **10b** (R^9=propyl) prepared by Method P (200 mg, 0.84 mmol) and HATU (319 mg, 0.84 mmol) were added and the mixture was stirred for 4 h at rt. DMF was removed and the residue was extracted with ethyl acetate (100 mL) and washed with saturated bicarbonate (40 mL). The product obtained by removal of solvent was taken up in methanol and treated with ~~Dowex~~ Dowex™ H^+ resin for 1 h. After filtering the resin, methanol was removed to obtain the crude product. The crude product was then purified on silica gel column using 10% methanol in dichloromethane as the eluent to provide pyridine **11b** (R^1=Me, R^2=Me, R^3=H, R^9=propyl) (117 mg, 58%).

Please replace paragraph **[0274]** with the following amended paragraph:

[0274] DIEA (0.1 mL, 0.57 mmol) and liquid ethylene oxide (3 mL) were added to a stirred solution of crude ~~1-(4-*n*-pentylpyrrolidin-2-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide, prepared as in Example 10 (237.4 mg), in anhydrous methanol (10 mL), at 0°C and under nitrogen. The resulting solution was stirred at -4°C for 18 h and evaporated to dryness. The residue obtained was purified by chromatography over silica gel with an eluent of 5% ~~methanol~~ methanolic ammonia in dichloromethane. The desired fractions were evaporated and the residue lyophilized (deuterium oxide/anhydrous acetonitrile, 1:1, v/v, 10mL) to furnish the title compound as a fluffy

white powder (50.1mg, 30.2%); TLC, R_f= 0.68 (14% methanolic ammonia in dichloromethane); ^{1}H NMR (300 MHz) δ 5.40 (d, J=5.8, 1), 4.55 (m, 1), 4.24 (s, 1), 4.17-4.11 (m, 1), 3.99-3.89 (m, 4), 3.69-3.65 (m, 1), 3.47 (d, J=4.4, 2), 3.01 (m, 1), 2.33 (br s,4), 2.18 (s,4), 1.57-1.32 (m,9), 0.94-0.87 (m, 9). MS(ESPOS):464[M+H];(ESNEG):497.5[M-H+HCl].

Please replace paragraph **[0275]** with the following amended paragraph:

[0275] DIEA (0.1mL, 0.58 mmol, 1 equiv) and R(+)-propylene oxide (3 mL) were added to a stirred cool solution of crude ~~1-(2-(S)-4-(R)-*n*-pentylpyrrolidin-2-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide (307.6 mg, 0.58 mmol, 1 equiv), prepared as in Example 10, in anhydrous methanol (10mL), at 0°C and under nitrogen. The resulting solution was stirred at -4°C for 18 h and evaporated to dryness. The residue obtained was purified by chromatography over silica gel, with an eluent of 6% ~~methanol~~ methanolic ammonia in dichloromethane. The desired fractions were evaporated, and lyophilized (deuterium oxide/anhydrous acetonitrile, 1:1, v/v, 20mL) to furnish the title compound as a fluffy white powder (91mg, 48%).

Please replace paragraph **[0277]** with the following amended paragraph:

[0277] Dimethyl sulfide (62 μL), TFA (1 mL), and water (62 μL) were added to a stirred solution of the Boc-protected ~~1-(2-(S)-4-(R)-*n*-pentylpyrrolidin-2-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide (92mg, 0.18 mmol), prepared as in Example 10, in anhydrous dichloroethane (3 mL). The resulting solution was stirred at rt for 1 h and evaporated to dryness. Anhydrous methanol (8 mL) and DIEA (31 μL, 0.18 mmol) were added to the residue obtained. The mixture was cooled to -4°C and S-(-)-propylene oxide (2 mL) was added. The resulting solution was stirred at -4°C for 18 h, evaporated to dryness, and purified by chromatography over silica gel, with an eluent of 6% ~~methanol~~ methanolic ammonia in dichloromethane. The desired fractions were evaporated and lyophilized

(deuterium/anhydrous acetonitrile, 1:1, v/v, 8 mL) to furnish the title compound as a fluffy white powder (29.8 mg, 31.2%).

Please replace paragraph **[0279]** with the following amended paragraph:

[0279] Triethylamine (0.2 mL, 1.38 mmol, 3 equiv), followed by 3-bromo-1-propanol (60 μL, 0.69 mmol, 1.5 equiv), were added to a stirred solution of crude ~~1-(2-(S)-4-(R)-*n*-pentylpyrrolidin-2-yl)-*N*-{1-(R)-[2-(S)-3-(S),-4-(S),-5-(R)-trihydroxy-6-(R)-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide (192.5 mg, 0.46 mmol, 1 equiv), prepared as in Example 10, in anhydrous acetonitrile (2 mL), under nitrogen. The resulting mixture was stirred at rt for 18 h and evaporated to dryness. The residue obtained was purified by chromatography over silica gel with an eluent of 5% ~~methanol~~ methanolic ammonia in dichloromethane. The desired fractions were pooled together, evaporated to dryness, and lyophilized to furnish the title compound as a white fluffy powder (13.5 mg, 6%).

Please replace paragraph **[0281]** with the following amended paragraph:

[0281] Ethylene oxide (0.6 mL) was added to a solution of ~~1-[2-(S)-4-(R)-(3-methylbut-1-yl)pyrrolidin-2-yl]-*N*-{1-(R)-[2-(S)-3-(S),-4-(S),-5-(R)-trihydroxy-6-(R)-(methylthio)-tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3-methyl-butyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide (35.1 mg, 0.084 mmol), prepared as in Example 9, in methanol (3 mL), at 0°C. The reaction mixture was stirred at 4°C overnight. Additional ethylene oxide (0.6 mL) was added and stirred at 4°C overnight. The reaction mixture was concentrated and purified by chromatography to give ~~a white solid, 1-[2-(S)-4-(R)-(3-methylbut-1-yl)-*N*-(2-hydroxyeth-1-yl)pyrrolidin-2-yl]-*N*-{1-(R)-[2-(S)-3-(S),-4-(S),-5-(R)-trihydroxy-6-(R)-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ the title compound as a white solid (24.1 mg, 62%).

Please replace paragraph **[0283]** with the following amended paragraph:

[0283] Ethylene oxide (0.4 mL) was added to a solution of ~~1-[2-(S)-4-(R)-(3,3-difluoroprop-1-yl)pyrrolidin-2-yl]-*N*-{1-(R)-[2-(S)-3-(S),-4-(S),-5-(R)-trihydroxy-6-(R)-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3,3-difluoro-propyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide, prepared as in Example 14 (29.7 mg, 0.07 mmol), in methanol (2 mL), at 0°C. The reaction mixture was stirred at 4°C overnight. Additional ethylene oxide (0.4 mL) was added and stirred at 4°C overnight. The reaction mixture was concentrated and purified by chromatography to give ~~a white solid, 1-[2-(S)-4-(R)-(3-methylbut-1-yl)-*N*-(2-hydroxyeth-1-yl)pyrrolidin-2-yl]-*N*-{1-(R)-[2-(S)-3-(S),-4-(S),-5-(R)-trihydroxy-6-(R)-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ the title compound as a white solid (19.3 mg, 59%).

Please replace paragraph **[0290]** with the following amended paragraph:

[0290] Then to 7-methyl α-thiolincosaminide **2b** (R^1=Me, R^2=Me) (90 mg, 0.35 mmol) in DMF (2ml), TEA (72 mg, 0.7 mmol), BSTFA (276 mg, 1.05 mmol) were added at 0 °C and stirred at room temperature for 1.5 hr. Then the acid (**10b**) (R^9=pentyl) (138 mg, 0.7 mmol) and HATU (165 mg, 0.53 mmol) was added to the reaction mixture, and stirred at room temperature overnight. DMF was completely removed, the residue was taken up in EtOAc (50 mL), washed with sodium bicarbonate (10%, 50 mL), brine (50 mL). The product obtained after drying over magnesium sulfate and concentration was taken up in methanol (10 mL) and treated with Dowex™ polymeric sulfonic acid H^+ ~~NR-50~~ resin (150 mg) for 3 hr. The resin was filtered and the solvent was removed. Purification of the crude product was carried out silica gel column chromatography using 3% MeOH in DCM as eluent to obtain compound **11b** (R^1=Me, R^2=Me R^3=H, R^9=pentyl) (90 mg, 59%):

Please replace paragraph **[0298]** with the following amended paragraph:

[0298] To 7-methyl α-thiolincosaminide, compound **2b** (R^1=Me, R^2=Me), (90 mg, 0.35 mmol) in DMF (2 mL), TEA (72 mg, 0.7 mmol), BSTFA (276 mg, 1.05 mmol) were added at 0°C and left stirred at room temperature for 1.5 hr. Then compound **10b** (R^9 = methoxy) (109 mg, 0.7 mmol) and

HATU (165 mg, 0.53 mmol) were added to the reaction mixture, and stirred at room temperature overnight. The DMF was completely removed and the residue was taken up in EtOAc (50 mL), washed with sodium bicarbonate (10%, 30 mL), brine (30 mL), and dried over magnesium sulfate. The solvent was removed to obtain a brown oil-like liquid, which was dissolved in methanol (10 mL) and treated with Dowex™ polymeric sulfonic acid H^+ ~~NR-50~~ resin for 1 hr. The resin was filtered, and the solvent was removed to obtain the crude material. Purification was carried out on silica gel column chromatography using EtOAc as eluent to obtain compound **11b** (R^1=Me, R^2=Me R^3=H, R^9=methoxy) (100 mg, 72%).

Please replace paragraph **[0313]** with the following amended paragraph:

[0313] To the amine, compound **2b** (R^1=Me, R^2=Me), (140 mg, 0.56 mmol) in DMF (3 mL), BSTFA (0.59 mL, 2.24 mmol) and triethylamine (0.18 mL, 1.26 mmol) were added at 0°C and the reaction mixture was stirred at room temperature for 3 hours. Acid **10b** (R^9 = isopropyl) (188 mg, 1.13 mmol) and HATU (319 mg, 0.84 mmol) were combined and left stirred for further 4 hours at room temperature. The DMF was removed and the residue was extracted with ethyl acetate (100 mL) and washed with saturated bicarbonate (40 mL). The product obtained on removal of solvent was taken up in methanol and treated with ~~Dowex~~ Dowex™ H^+ resin for 1 hour. After filtering the resin, methanol was removed to obtain the crude product. It was then purified on silica gel column using 10% methanol in dichloromethane as eluent to provide compound **11b** (R^1=Me, R^2=Me R^3=H, R^9 = isopropyl) (120 mg, 53 %).

Please replace paragraph **[0321]** with the following amended paragraph:

[0321] To the amine, compound **2b** (R^1=Me, R^2=Me), (140 mg, 0.56 mmol) in DMF (3 mL), BSTFA (0.59 mL, 2.24 mmol) and triethylamine (0.18 mL, 1.26 mmol) were added at 0 °C and then stirred at room temperature for 3 hours. Acid **10b** (R^9 = butyl) (203 mg, 1.13 mmol) and HATU (319 mg, 0.84 mmol) were added and the reaction mixture was stirred for 4 more hours at room temperature. The DMF was removed and the residue was extracted with ethyl acetate (100 mL) and washed with saturated bicarbonate (40 mL). The product obtained on removal of solvent was taken up in methanol and treated with ~~Dowex~~ Dowex™ H^+ resin for 1 hour. After filtering the resin,

methanol was removed to obtain the crude product. The product was then purified on silica gel column using ethyl acetate as eluent to provide for compound **11b** (R^1=Me, R^2=Me R^3=H, R^9 = butyl) (200 mg, 86 %).

Please replace paragraph **[0327]** with the following amended paragraph:

[0327] To the amine **2b** (R^1=Me, R^2=Me) (102 mg, 0.42 mmol) in DMF (5 mL), BSTFA (0.549 mL, 2.1 mmol) and triethylamine (0.183 mL, 1.26 mmol) was added at 0 °C and then stirred at room temperature for 3 hours. Acid **10b** (R^9=phenyl) (158 mg, 0.80 mmol) and HATU (302 mg, 0.80 mmol) were added and the reaction was stirred for an additional 4 hours at room temperature. The DMF was removed and the residue was extracted with ethyl acetate (100 mL) and washed with saturated bicarbonate (40 mL). The product obtained on removal of solvent was taken up in methanol and treated with ~~Dowex~~ Dowex™ H^+ resin for 1 hour. After filtering the resin, methanol was removed to obtain the crude product. The resulting residue was then purified by silica gel chromatography using 10% methanol in dichloromethane as eluent to provide compound **11b**(R^1=Me, R^2=Me R^3=H, $R^{9'}$ = phenyl) (50 mg, 58 %).

Please replace paragraph **[0374]** with the following amended paragraph:

[0374] To a solution of the ~~product~~ title compound of Example [[**42**]] **39** (17.9 mg, 0.039 mmol) in MeOH (2 mL) at 0 °C was added ethylene oxide (0.4 mL). The reaction mixture was stirred at 4 °C overnight. The reaction mixture was concentrated and purified by chromatography to give the title compound as a white solid (8.2 mg, 42%).

Please replace paragraph **[0377]** with the following amended paragraph:

[0377] Compound **14c** (R^9 = ~~2,2-difluoroethyl~~ 3,3-difluoro-propyl) is prepared using the methods described in general Method R.

Please replace paragraph **[0385]** with the following amended paragraph:

[0385] To a solution of 4-(3,3-difluoro-propyl)-pyridine-2-carboxylic acid methyl ester (130 mg, 0.6 mmol) ([[or]] compound **14c** [[(]]R^9 = 3,3-difluoro-propyl ~~2,2-difluoroethyl~~) ~~prepared in the~~

~~previous steps)~~ in MeOH (3 mL) and water (3 mL) were added conc. HCl (0.25 mL, 3.0 mmol, 5 equiv) and platinum oxide (65 mg). The mixture was purged and charged with hydrogen (1 atm) and stirred overnight. The platinum oxide was removed by filtration and the filtrate was evaporated to give a clear syrup. To the above residue were added 2N NaOH (1.21 mL) and *t*-butyl alcohol (0.7 mL). The mixture was stirred at rt for 2 hrs. Then di-*t*-butyl dicarbonate (0.16 g, 0.73 mmol) was added. The mixture was stirred at rt overnight. The solvent was removed under vacuum. The residue was diluted with water (10 mL), was washed with ether (20 mL). The aqueous layer was acidified with 2N HCl to pH = 2.0, and extracted with ethyl acetate (2x). The combined organic layers were dried and concentrated to give 4-(3,3-[[D]]difluoro-propyl)-piperidine-1,2-dicarboxylic acid 1-*tert*-butyl ester as a clear syrup (163 mg, 88 %).

Please replace paragraph **[0398]** with the following amended paragraph:

[0398] To a mixture of the HCl salt of compound **2b** (R^1=Me, R^2=Me) (153 mg, 0.53 mmol, 1 equiv) in dry DMF (1.3 mL) at 0° C was added triethylamine (0.37 mL, 2.66 mmol, 5 equiv), followed by the addition of BSTFA (0.21 mL, 0.80 mmol, 1.5 equiv). The reaction mixture was stirred at 0° C for 10 minutes, and then was stirred at rt for 50 minutes. To the reaction mixture were added the 4-(4,4-difluoro-butyl)-piperidine-1,2-dicarboxylic acid 1-*tert*-butyl ester (196 mg, 0.61 mmol, 1.15 equiv) and HATU (293 mg, 0.77 mmol, 1.45 equiv). The reaction mixture was stirred at rt for 3 h. The reaction mixture was evaporated to dryness, taken up in ethyl acetate, washed with 10% citric acid (1x), water (1x), sat. $NaHCO_3$ (1x) and brine. The organic layer was dried over Na_2SO_4 and evaporated to give the crude product as a syrup. The residue was dissolved in methanol (20 mL), then dried and washed ~~Dowex~~ Dowex™ resin (100 mg) was added. The mixture was stirred at rt for 30 minutes, and filtered. The filtrate was concentrated to give a clear syrup, which was purified by chromatography to give a clear syrup (0.25g, 85 %).

Please replace paragraph **[0414]** with the following amended paragraph:

[0414] To a mixture of the HCl salt of compound **2b** (R^1=Me, R^2=Me) (223.7 mg, 0.78 mmol, 1 equiv) in dry DMF (1.9 mL) at 0° C was added triethylamine (0.54 mL, 3.89 mmol, 5 equiv), followed by the addition of BSTFA (0.31 mL, 1.17 mmol, 1.5 equiv). The reaction mixture was

stirred at 0° C for 10 minutes, and then was stirred at rt for 50 minutes. To the reaction mixture were added 4-(5,5-difluoro-pentyl)-piperidine-1,2-dicarboxylic acid 1-*tert*-butyl ester (272 mg, 0.81 mmol, 1.05 equiv) and HATU (391 mg, 1.03 mmol, 1.32 equiv). The reaction mixture was stirred at rt for 3 h. The reaction mixture was evaporated to dryness, taken up in ethyl acetate, washed with 10% citric acid (1x), water (1x), sat. $NaHCO_3$ (1x) and brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue. The residue was dissolved in methanol (30 mL), then dry and washed ~~Dowex~~ Dowex™ resin (150 mg) was added. The mixture was stirred at rt for 1 h and filtered. The filtrate was concentrated to give a clear syrup, which was purified by chromatography to give a clear syrup (0.26 g, 72 %).

Please replace paragraph **[0423]** with the following amended paragraph:

[0423] To a mixture of the HCl salt of compound **2b** (R^1=Me, R^2=Me) (213.8 mg, 0.74 mmol, 1 equiv) in dry DMF (1.8 mL) at 0 °C was added triethylamine (0.52 mL, 3.72 mmol, 5 equiv), followed by the addition of BSTFA (0.30 mL, 1.12 mmol, 1.5 equiv). The reaction mixture was stirred at 0 °C for 10 minutes, and then was stirred at rt for 50 minutes. To the reaction mixture were added the 4-(5-fluoro-pentyl)-piperidine-1,2-dicarboxylic acid 1-*tert*-butyl ester as a syrup (244 mg, 0.77 mmol, 1.04 equiv) and HATU (370 mg, 0.97 mmol, 1.31 equiv). The reaction mixture was stirred at rt for 3 h. The reaction mixture was evaporated to dryness, taken up in ethyl acetate, washed with 10% citric acid (1x), water (1x), sat. $NaHCO_3$ (1x) and brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue. The residue was dissolved in methanol (30 mL), then dry and washed ~~Dowex~~ Dowex™ resin (140 mg) was added. The mixture was stirred at rt for 1 h and filtered. The filtrate was concentrated to give a clear syrup, which was purified by chromatography to give a clear syrup (212 mg, 52 %).

Please replace paragraph **[0450]** with the following amended paragraph:

[0450] The title compound was made using the synthetic sequence found in general Method S starting from 4-hydroxypyridine-2-carboxylic acid **10b** (R^9 = hydroxy) substituting 1-bromo-4-fluoro-butane ~~4-fluorobutyl bromide~~ as the alkylating agent.

Please replace paragraph **[0452]** with the following amended paragraph:

[0452] To a solution of Boc 7-Methylene MTL (P=Boc, R^1=Me, [[R^2]] $\underline{R^{2'}}$ =CH_2) prepared from compound **2a** (P=Boc, R^1=Me) by general Method D (391mg, 1.1 mmol) in a solution of dichloroethane (10 mL) and dimethylsulfide (0.4 mL, 2.5 mmol) was added, TFA (5 mL) containing water (0.4 mL) and the reaction mixture stirred at rt for 45min. The solvent was removed and the residue evaporated twice from DCE to obtain the crude product. The product was obtained as an HCl salt by precipitation from ethyl acetate (4 mL) at 0 °C by addition of 2M HCl in ether, and dried under vacuum (351mg g, 86%). The white solid product was used in the next reaction without additional purification.

Please replace paragraph **[0459]** with the following amended paragraph:

[0459] The title compound was made using the synthetic sequence found in general Method S starting from 4-hydroxypyridine-2-carboxylic acid substituting <u>1-bromo-3-fluoro-propane</u> ~~3-fluoropropyl bromide~~ as the alkylating agent.

Please replace paragraph **[0463]** with the following amended paragraph:

[0463] The title compound was made using the synthetic sequence found in general Method S starting from 4-hydroxypyridine-2-carboxylic acid substituting <u>3-bromo-1,1,1-trifluoro-propane</u> ~~2-trifluoroethyl bromide~~ as the alkylating agent.

Please replace paragraph **[0470]** with the following amended paragraph:

[0470] To the amine **2b** (R^1=Me, R^2=Me) (200 mg, 0.79 mmol) in DMF (2ml), TEA (161 mg, 1.6 mmol), BSTFA (614 mg, 2.4 mmol) was added at 0 °C and stirred at room temperature for 1.5 hr. Acid **10b** (R^9 = isobutyl) (214 mg, 1.2 mmol) and HATU (368 mg, 1.2 mmol) was added and let stirred at room temperature for 4 hours. DMF was removed and the residue was extracted with EtOAc (50 mL), washed with sodium bicarbonate (10%, 50 mL), brine (50 mL) and dried over magnesium sulfate. The product obtained on removal of solvent was dissolved in methanol (10 mL) and treated with <u>Dowex™ polymeric sulfonic acid H^+</u> ~~NR-50~~ resin (300 mg) for 3 hr. After filtering the resin, methanol was removed to obtain the crude product. It was then purified on silica gel

column chromatography using 3% MeOH in DCM to obtain compound **11b** (R^1=Me, R^2=Me, R^3=H, R^9=isobutyl) (200 mg, 60%).

Please replace paragraph **[0476]** with the following amended paragraph:

[0476] To a stirred solution of (2S, 4R)-4-hydroxyproline (Aldrich) (25 g, 108 mmol) in methanol (50 mL) at 0 °C was added trimethylsilyldiazomethene (24.6 g, 216 mmol). The mixture was stirred at 0 °C for 1 hour. The residue obtained on removal of solvent and purification by column chromatography using 50% ethyl acetate in hexanes (27 g, 100%) was used in the next step. To oxalyl chloride (15 g, 118 mmol) in DCM (15 mL) at -78 °C, DMSO (18.6 mL, 236 mmol) was added slowly over 15 minutes. After the completion of addition, the above product (2S, 4R)-N-Boc-4-hydroxyproline methylester (26.5 g, 108 mmol) in DCM (100 mL) was added at -78 °C [[for]] dropwise over 20 minutes. Triethylamine (54.6 g, 540 mmol) was added followed by stirring at room temperature for 2 hours. The reaction mixture was then washed with 10% aq HCl (200 mL) and the organic layer was separated and dried over sodium sulfate. The crude product obtained on removal of solvent was purified on silica gel column chromatography using 50% EtoAc in hexanes to obtain 4-oxo-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester ~~(2S, 4R) N-Boc-4-Ketoproline methylester~~ (20 g, 78%).

Please replace paragraph **[0478]** with the following amended paragraph:

[0478] To a stirred solution of 4-oxo-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester ~~(2S, 4R) N-Boc-4-Ketoproline methylester~~ (1 g, 4.11 mmol) in THF (10 mL), tetraallyltin (1.08 mL, 4.52 mmol) in dry THF was added, then cooled to 0 °C before borontrifluoride etherate (0.520 mL, 4.11 mmol) was added drop wise. The mixture was stirred at 0 °C for 1h and then at room temperature for an additional 2 hours. Potassium fluoride (360 mg in 5mL water) and celite (1 g) was added and the reaction mixture was stirred for an hour. The reaction mixture was filtered and concentrated to dryness and the residue was dissolved in DCM (200 mL), washed with water (100mL) and brine 100 mL), dried over $MgSO_4$ and evaporated to dryness. T he residue obtained on removal of solvent was purified by silica gel column chromatography using 50% EtOAc in hexanes to obtain 4-allyl-4-hydroxy-pyrrolidine-1,2-

dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester ~~4-Hydroxy-4-allylproline methylester~~ (0.94 g, 80%).

Please replace paragraph **[0480]** with the following amended paragraph:

[0480] To a stirred solution of DAST (1.06 g, 6.58 mmol) in DCM (10 mL) at -78 °C, 4-allyl-4-hydroxy-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester ~~4-hydroxy-4-allylproline methylester~~ (940 mg, 3.3 mmol) in dry DCM (10 mL) was added slowly. The mixture was then stirred at -78 °C for 1h, then at -10 °C for an additional 1h. DCM (50 mL) was added, quenched with NH_4Cl (10%, 150 mL) and the organic layer was separated, dried over sodium sulfate and evaporated to dryness. The residue obtained on removal of solvent was purified by silica gel column chromatography using 5% EtOAc in hexanes as eluent to obtain 4-allyl-4-fluoro-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester ~~4-fluoro-4-allylproline methylester~~ (330 mg, 34%).

Please replace paragraph **[0482]** with the following amended paragraph:

[0482] To a solution of 4-allyl-4-fluoro-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester ~~4-fluoro-4-allylproline methylester~~ (0.33 g, 1.15 mmol) in MeOH (15 mL) was added 10% Pd/C (40 mg) and hydrogenated at 1 atmosphere. The catalyst was removed by filtration ~~filtered~~ through celite and washed with methanol. To the product obtained on removal of solvent (330 mg, 1.15 mmol) in THF (12 mL) was added [[aq]] lithium hydroxide monohydrate (60 mg, 1.38 mmol). The reaction mixture was stirred at room temperature overnight. THF was removed and the residue was taken up in ethyl acetate (50 mL), washed with 10% citric acid (100 mL) and brine (20 mL). Removal of solvent resulted in 4-allyl-4-propyl-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester ~~4-fluoro-4-propylproline~~ (310 mg, 100%).

Please replace paragraph **[0484]** with the following amended paragraph:

[0484] To a solution of 4-allyl-4-propyl-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester ~~4-fluoro-4-propylproline~~ (310 mg, 1.15 mmol) in DMF (3 mL) at 0 °C, 7-Methyl MTL **2b** (R^1 =Me, R^2=Me) (272 mg, 1.15 mmol), HBTU (469 mg, 1.3 mmol) and DIEA (290 mg, 2.3 mmol) was

added, left stirred at room temperature for 16 hours. DMF was removed and the residue obtained was purified by 3% MeOH in DCM(40 mg, 93%). The product from the column purification was taken in DCE (6 mL), to which triethylsilane (0.16 mL), TFA (2 mL) and water (0.16 mL) was added and stirred at room temperature for 1.5 hours. Removal of solvent followed by purification on silica gel column chromatography using 10% MeOH in DCM resulted in the title compound as isomeric mixtures with lower [[RF]]R_f fraction (160 mg, 50%).

Please replace paragraph **[0486]** with the following amended paragraph:

[0486] To ethyl acetylene (140 mg, 2.6 mmol) in THF (5 mL) at –78 °C, n-butyllithium (1.1 mL, 2.6 mmol) was added with stirring at –78 °C for 1 hour. Then 4-oxo-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester ~~n-(tert-Butoxycarbonyl)-L-proline-4-ketone~~ (prepared as described in the example 56) (570 mg, 2.3 mmol) in THF (5 mL) was added at –78 °C with stirring for 2 h, the reaction mixture was then allowed to ~~hours and then let it~~ warm to –40 °C over 1 hour. The reaction mixture was extracted with EtOAc (20 mL), washed with saturated NH_4Cl (5 mL) and dried over sodium sulfate. Purification of the crude product was carried out by silica gel chromatography using 50% EtOAc in hexane to obtain the 4-butyl-4-hydroxy-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester ~~N-boc-4-butyl-4-hydroxy-prolinemethyl ester~~ (520 mg, 73%). To the DAST (556 mg, 3.4 mmol) in DCM (5 mL) at –78 °C, was added a solution of the above ester (520 mg, 1.7 mmol) in DCM (5 mL) at –78 °C and stirred for 1 hour. The reaction mixture was extracted with DCM (50 mL) and washed with $NaHCO_3$ (30 mL, 10%). The product obtained after removal of solvent was purified by silica gel chromatography using 5% EtOAc in hexanes to obtain 4-butyl-4-fluoro-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester ~~N-(tert-butoxycarbonyl)-L-proline-4-fluoro-4-butane~~ (276 mg, 52%).

Please replace paragraph **[0488]** with the following amended paragraph:

[0488] To a solution of 4-butyl-4-fluoro-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester ~~N-(tert-butoxycarbonyl)-L-proline-4-fluoro-4-butane~~ (270 mg, 0.89 mmol) in THF (12 mL) and water (4 mL), was added lithium hydroxide monohydrate (45 mg, 1.07 mmol). The reaction mixture was stirred at room temperature for 16 hours. THF was removed under vacuum

and the residue was taken up in ethyl acetate (150 mL), washed with 10% citric acid (100 mL) and brine (20mL). Removal of solvent provided 4-butyl-4-fluoro-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester ~~resulted in N-(tert-butoxy)-L-proline-4-fluoro-4-butyl-2-carboxylic acid~~ (260 mg, 100%).

Please replace paragraph **[0490]** with the following amended paragraph:

[0490] To a solution of 4-butyl-4-fluoro-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester ~~N-(tert-butoxy)-L-proline-4-fluoro-4-butyl-2-carboxylic acid~~ (135 mg, 0.46 mmol) in DMF (3 mL) at 0 °C, 7-Methy MTL **2b** (R^1 =Me, R^2=Me) (135 mg, 0.46 mmol), HBTU (194 mg, 0.51 mmol), DIEA (120 mg, 0.93 mmol) was added, left it at room temperature for 16 hours. The product obtained after removing DMF and purification by column chromatography using 5% MeOH in DCM (189 mg, 77%) was taken in DCE (6 mL). Triethylsilane (0.16 mL), TFA (2 mL) and water (0.16 mL) was added, stirred at room temperature for 1.5 hours. The residue obtained on removal of solvent was purified by column chromatography using 10% MeOH in DCM to obtain the title compound (156 mg, 96%).

Please replace paragraph **[0494]** with the following amended paragraph:

[0494] The title compound was made using the synthetic sequence found in general Method S starting from 4-hydroxypyridine-2-carboxylic acid, substituting 1-bromo-2-methoxy-ethane ~~2-methoxyethyl bromide~~ as the alkylating agent.

Please amend the abbreviation designation on page 43, line 14 as follows:

d [[D]]	=	Doublet

Please amend the abbreviation designation on page 44, line 11 as follows:

min [[Min]]	=	minutes

Please amend the abbreviation designation on page 44, line 13 as follows:

mm [[Mm]] = millimeter

On page 61, please amend the title for Example 1 as follows:

Example 1

Preparation of ~~1-(4-ethylpiperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-Ethyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 62, please amend the title for Example 2 as follows:

Example 2

Preparatiaon of ~~1-(4-*n*-propyl-*N*-methylpyrrolidin-2-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio_tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
1-Methyl-4-propyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 63, please amend the title for Example 3 as follows:

Example 3

Preparation of ~~1-(-4-*n*-propyl-N-methylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methyl-3-cyanoprop-1-yl}acetamide~~
1-Methyl-4-propyl-pyrrolidine-2-carboxylic acid [3-cyano-2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 64, please amend the title for Example 4 as follows:

Example 4

Preparatiaon of ~~1-(-4-ethylpiperidyl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-hydroxy-2-methylprop-1-yl}acetamide~~
4-Ethyl-piperidine-2-carboxylic acid [2-hydroxy-2-methyl-1-(3,4,5-tridroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 65, please amend the title for Example 5 as follows:

Example 5

Preparation of ~~1-(-4-*n*-propyl-*N*-methylpyrrolidin-2-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-hydroxyiminoprop-1-yl}acetamide~~ 1-Methyl-4-propyl-pyrrolidine-2-carboxylic acid [2-hydroxyimino-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 66, please amend the title for Example 6 as follows:

Example 6

Preparation of ~~1-(-4-*n*-propyl-*N*-methylpyrrolidin-2-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methoxyiminoprop-1-yl}acetamide~~ 1-Methyl-4-propyl-pyrrolidine-2-carboxylic acid [2-methoxyimino-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 66, please amend the title for Example 7 as follows:

Example 7

Preparation of ~~1-(-3-n-butylpiperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 5-Butyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 67, please amend the title for Example 8 as follows:

Example 8

Preparation of ~~1-(4-(R,S)-n-pentylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-Pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 68, please amend the title for Example 9 as follows:

Example 9

Preparation of ~~1-[4-(3-methylbut-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3-Methyl-butyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 69, please amend the title for Example 10 as follows:

Example 10

Preparation of ~~1-(-4-n-pentylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-Pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 70, please amend the title for Example 11 as follows:

Example 11

Preparation of ~~1-(-4-n-propyl-N-methylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2,2-difluoroprop-1-yl}acetamide~~ 1-Methyl-4-propyl-pyrrolidine-2-carboxylic acid [2,2-difluoro-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 71, please amend the title for Example 12 as follows:

Example 12

Preparation of ~~1-(-4-n-pentylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2,2-difluoroprop-1-yl}acetamide~~

4-Pentyl-pyrrolidine-2-carboxylic acid [2,2-difluoro-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 72, please amend the title for Example 13 as follows:

Example 13

Preparation of ~~1-(-4-(3-p-fluorophenyl)prop-1-ylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-[3-(4-Fluoro-phenyl)-propyl]-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 73, please amend the title for Example 14 as follows:

Example 14

Preparation of ~~1-[2-(S)-4-(R)-(3,3-difluoroprop-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-(3,3-Difluoro-propyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 74, please amend the title for Example 15 as follows:

Example 15

Preparation of ~~1-(-4-(3-p-chlorophenyl)prop-1-ylpyrrolidin-2-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-[3-(4-Chloro-phenyl)-propyl]-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 75, please amend the title for Example 16 as follows:

Example 16

Preparation of ~~1-[2-(S)-4-(S)-(2,2-difluoropent-1-yl)pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-(2,2-Difluoro-pentyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 76, please amend the title for Example 17 as follows:

Example 17

Preparation of ~~1-(4-n-propylpiperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide
4-Propyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 77, please amend the title for Example 18 as follows:

Example 18

Preparation of ~~1-[2-(S)-4-(R)-*n*-pentyl-*N*-(2-hydroxyeth-1-yl)pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide
1-(2-Hydroxy-ethyl)-4-pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 77, please amend the title for Example 19 as follows:

Example 19

Preparation of ~~1-[2-(S)-4-(R)-*n*-pentyl-*N*-(2-(R)-methyl-2-hydroxyeth-1-yl)pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide
1-(2-Hydroxy-propyl)-4-pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 78, please amend the title for Example 20 as follows:

Example 20

Preparation of ~~1-[2-(S)-4-(R)-*n*-pentyl-*N*-(2-(S)-methyl-2-hydroxyeth-1-yl)pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide
1-(2-Hydroxy-propyl)-4-pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylslfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 79, please amend the title for Example 21 as follows:

Example 21

Preparation of ~~1-(4-*n*-pentyl-*N*-(3-hydroxyprop-1-yl)pyrrolidin-2-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 1-(3-Hydroxy-propyl)-4-pentyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 80, please amend the title for Example 22 as follows:

Example 22

Preparation of ~~1-[2-(S)-4-(R)-(3-methylbut-1-yl)-*N*-(2-hydroxyeth-1-yl)pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 1-(2-Hydroxy-ethyl)-4-(3-methyl-butyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 81, please amend the title for Example 23 as follows:

Example 23

Preparation of ~~1-[4-(3,3-difluoroprop-1-yl)-*N*-(2-hydroxyeth-1-yl)pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3,3-Difluoro-propyl)-1-(2-hydroxy-ethyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 82, please amend the title for Example 24 as follows:

Example 24

Preparation of ~~1-[2-(S)-4-(R)-n-pentyl-N-(2-hydroxyeth-1-yl)pyrrolidin-2-yl]-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2,2-difluoroprop-1-yl}acetamide~~ 1-(2-Hydroxy-ethyl)-4-pentyl-pyrrolidine-2-carboxylic acid [2,2-difluoro-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 82, please amend the title for Example 25 as follows:

Example 25

Preparation of ~~1-(4-*n*-pentylpiperid-6-yl)-*N*-{[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-Pentyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 84, please amend the title for Example 26 as follows:

Example 26

Preparation of ~~1-(4-methoxypiperid-6-yl)-*N*-{[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-Methoxy-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 85, please amend the title for Example 27 as follows:

Example 27

Preparation of ~~1-[4-(1-ethylprop-1-yl)piperid-6-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-(1-Ethyl-propyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 87, please amend the title for Example 28 as follows:

Example 28

Preparation of ~~1-(4-iso-propylpiperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-Isopropyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 88, please amend the title for Example 29 as follows:

Example 29

Preparation of ~~1-(4-*n*-butylpiperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-Butyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 90, please amend the title for Example 30 as follows:

Example 30

Preparation of ~~1-(4-cyclohexylpiperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-Cyclohexyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 92, please amend the title for Example 31 as follows:

Example 31

Preparation of ~~1-(4-ethyl-*N*-hydroxyethyl-piperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-Ethyl-1-(2-hydroxy-ethyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 92, please amend the title for Example 32 as follows:

Example 32

Preparation of ~~1-(4-*n*-pentyl-*N*-hydroxyethyl-piperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
1-(2-Hydroxy-ethyl)-4-pentyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 93, please amend the title for Example 33 as follows:

Example 33

Preparation of ~~1-(4-*n*-propyl-*N*-hydroxyethyl-piperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
1-(2-Hydroxy-ethyl)-4-propyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 93, please amend the title for Example 34 as follows:

Example 34

Preparation of ~~1-[4-*n*-propyl-*N*-(F-moc)-piperid-6-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 2-[2-Methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propylcarbamoyl]-4-propyl-piperidine-1-carboxylic acid 9*H*-fluoren-9-ylmethyl ester

On page 94, please amend the title for Example 35 as follows:

Example 35

Preparation of ~~1-[4-*n*-propyl-*N*-(carboxylic acid ethyl ester)-piperid-6-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 2-[2-Methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propylcarbamoyl]-4-propyl-piperidine-1-carboxylic acid ethyl ester

On page 95, please amend the title for Example 36 as follows:

Example 36

Preparation of ~~1-[4-*n*-propyl-*N*-(carboxylic acid phenyl ester)-piperid-6-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 2-[2-Methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propylcarbamoyl]-4-propyl-piperidine-1-carboxylic acid phenyl ester

On page 95, please amend the title for Example 37 as follows:

Example 37

Preparation of ~~1-[4-(4,4-difluoropent-1-yl) pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(4,4-Difluoro-pentyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 98, please amend the title for Example 38 as follows:

Example 38

Preparation of ~~1-[4-(3,3-difluorobut-1-yl)pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3,3-Difluoro-butyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 100, please amend the title for Example 39 as follows:

Example 39

Preparation of ~~1-[4-(3,3-difluoropent-1-yl)pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-(3,3-Difluoro-pentyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 102, please amend the title for Example 40 as follows:

Example 40

Preparation of ~~1-[4-(3,3-difluoropent-1-yl)-*N*-(2-hydroxyeth-1-yl)pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-(3,3-Difluoro-pentyl)-1-(2-hydroxy-ethyl)-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 102, please amend the title for Example 41 as follows:

Example 41

Preparation of ~~1-(4-(2,2-difluoroeth-1-yl)piperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-(3,3-Difluoro-propyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 105, please amend the title for Example 42 as follows:

Example 42

Preparation of ~~1-(4-(3,3-difluoroprop-1-yl)piperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-(4,4-Difluoro-butyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 107, please amend the title for Example 43 as follows:

Example 43

Preparation of ~~1-(4-(5,5-difluoropent-1-yl)piperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(5,5-Difluoro-pentyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 110, please amend the title for Example 44 as follows:

Example 44

Preparation of ~~1-(4-(5-fluoropent-1-yl)piperid-6-yl)-N-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(5-Fluoro-pentyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 112, please amend the title for Example 45 as follows:

Example 45

Preparation of ~~1-(4-(4-fluorobut-1-yl)piperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(4-Fluoro-butyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 113, please amend the title for Example 46 as follows:

Example 46

Preparation of ~~1-(4-(3-ethyl-3-hydroxypent-1-yl)piperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3-Ethyl-3-hydroxy-pentyl)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 114, please amend the title for Example 47 as follows:

Example 47

Preparation of ~~1-(4-butoxypiperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-Butoxy-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 116, please amend the title for Example 48 as follows:

Example 48

Preparation of ~~1-(4-pentoxypiperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide
4-Pentyloxy-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 117, please amend the title for Example 49 as follows:

Example 49

Preparation of ~~1-(4-(4-fluorobutoxy)piperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide
4-(4-Fluoro-butoxy)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 117, please amend the title for Example 50 as follows:

Example 50

Preparation of ~~1-[4-*n*-butylprop-1-yl)pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methyl-allyl}acetamide~~
4-Butyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-allyl]-amide

On page 119, please amend the title for Example 51 as follows:

Example 51

Preparation of ~~1-(4-ethyl-*N*-ethyl-piperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
1,4-Diethyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 119, please amend the title for Example 52 as follows:

Example 52

Preparation of ~~1-(4-(3-fluoropropoxy)piperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3-Fluoro-propoxy)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 120, please amend the title for Example 53 as follows:

Example 53

Preparation of ~~1-(4-(3,3,3-trifluoropropoxy)piperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-(3,3,3-Trifluoro-propoxy)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 121, please amend the title for Example 54 as follows:

Example 54

Preparation of ~~1-(4-*iso*-butylpiperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~ 4-Isobutyl-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 123, please amend the title for Example 55 as follows:

Example 55

Preparation of ~~1-(4-*n*-propylpiperid-6-yl)-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2,2-difluoro-prop-1-yl}acetamide~~ 4-Propyl-piperidine-2-carboxylic acid [2,2-difluoro-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 124, please amend the title for Example 56 as follows:

Example 56

Preparation of ~~1-[4-*n*-propyl-4-fluoro-pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-Fluoro-4-propyl-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 126, please amend the title for Example 57 as follows:

Example 57

Preparation of ~~1-[4-*n*-butyl-4-fluoro-pyrrolidin-2-yl]-*N*-{1-[3,4,5-trihydroxy-6-(methylthio)tetrahydropyran-2-yl]-2-methylprop-1-yl}acetamide~~
4-Butyl-4-fluoro-pyrrolidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide

On page 128, please amend the title for Example 59 as follows:

Example 59

Preparation of ~~4-propyl-pyrrolidine-2-carboxylic acid [2-hydroxy-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide~~
4-(2-methoxyethoxy)-piperidine-2-carboxylic acid [2-methyl-1-(3,4,5-trihydroxy-6-methylsulfanyl-tetrahydro-pyran-2-yl)-propyl]-amide